HYPERGLYCEMIA IN ACUTE ALUMINIUM PHOSPHIDE POISONING AS A POTENTIAL PROGNOSTIC FACTOR

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M.D DEGREE (BRANCH - I) GENERAL MEDICINE

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CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled **"HYPERGLYCEMIA IN ACUTE ALUMINIUM PHOSPHIDE POISONING AS A POTENTIAL PROGNOSTIC FACTOR"** is the bonafide work of **Dr. M.ANBARASAN,** in partial fulfilment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for M.D General Medicine, Branch I examination to be held in May 2018.

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DECLARATION

I, **Dr.M.ANBARASAN**, solemnly declare that this dissertation titled **"HYPERGLYCEMIA IN ACUTE ALUMINIUM PHOSPHIDE POISONING AS A POTENTIAL PROGNOSTIC FACTOR"** is a bonafide record of work done by me at the Department Of General Medicine, Government Rajaji Hospital, Madurai, under the guidance of **Dr.C.DHARMARAJ, M.D, DCH.,** Professor, Department of General Medicine, Madurai Medical college , Madurai.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfilment of the rules and regulations for the award of M.D Degree General Medicine Branch- I examination to be held in May 2018.

Place: Madurai **Dr.M.ANBARASAN**

Date:

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CONTENTS

INTRODUCTION

Since the first available report of AlP poisoning in the early 1980s from India, it is now one of the most common cause of poisoning among agricultural pesticides. Unfortunately the absence of a specific antidote results in very high mortality and the key to treatment lies in rapid decontamination and institution of resuscitative measures. AlP also poses as a threat for chemical terrorism due to the immediate release of lethal phosphine gas. Previously, the laws and legislations were not that strict and it was easily available on the counter; but in the last few years stricter norms have reduced its easy availability, even though they are still not enough to reduce the suicidal rate due to its consumption, which traumatizes so many families

Phosphides are used throughout the world as pesticides to protect stored grains from rodents and pests. In India ,especially in south india, aluminium phosphide (AlP) is accessible as 3-g tablets that are a combination of 56% AlP (total dose of 1,680 mg) and 44% ammonium carbonate. In the past 35 years, high mortality rates have been reported following significant exposures to aluminium, zinc or calcium phosphides. Exposure is rarely accidental with the majority of cases involving intentional acts of suicides. After ingestion, solid phosphide

including AlPs produce a toxic phosphine gas following any contact with water, moisture in the air, or hydrochloric acid in the stomach. Although the exact mechanism has not been well defined, it has been demonstrated that phosphine acts at the mitochondrial level, and once systematically absorbed, it will interfere with synthesis of enzymes and proteins. In addition to the corrosive action of phosphine, the mechanism of toxicity includes formation of highly reactive hydroxyl radicals. Cellular injury due to lipid peroxidation is also suggested. Previously, a reduction in the level of catalase and rise in the activity of superoxide dismutase in patients of AlP poisoning have been reported. The reduction of glutathione concentration in different tissues in AlP poisoning also explains the cellular injury, as glutathione is a protecting factor against oxidation by catalyzing the reduction of the oxygen peroxide in O2 and H2O.

Indicators of oxidative stress (reduced glutathione and malondialdehyde) are showed to reach peak levels within 48 h of exposure to poison. To our knowledge, there is paucity of data regarding measurement of total antioxidant capacity in patients with AlP poisoning although presence of phosphine-induced oxidative damage in animal studies has been well established. Moreover, any decrease in plasma levels of thiol groups, as an important part of antioxidant defense system, might imply the presence of oxidative stress in an AlP-poisoned patient.

This might result in generation of free radical and alteration in antioxidant system. Hence, this study was conducted to evaluate the existence of prognostic significance of High Blood Sugar Value in acute aluminium poisoning on admission.

AIM AND OBJECTIVES

The main goal of this study was to evaluate the prognostic significance of High Blood Sugar Value in acute aluminium poisoning on admission.

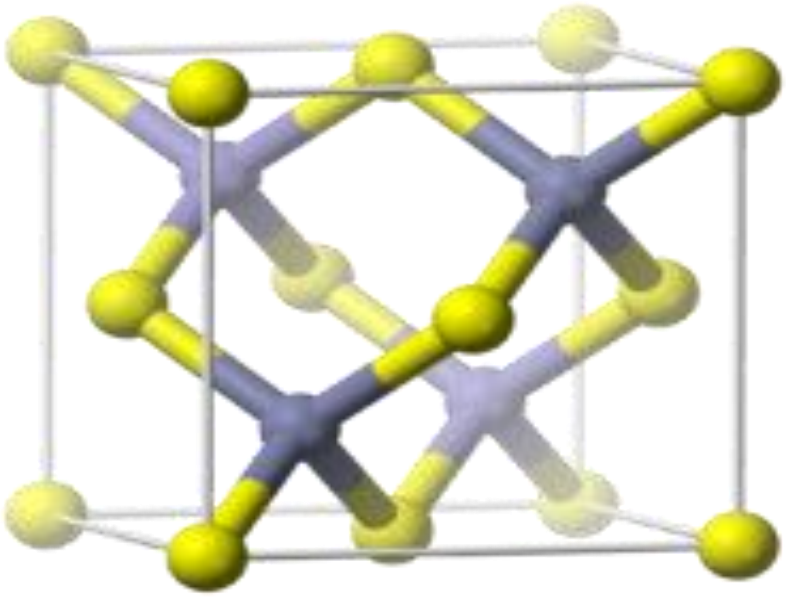
REVIEW OF LITERATURE

Phosphine (PH3) was discovered in the late 1700s and has been used as a grain fumigant since the 1930s. It is by far the dominant means of controlling pest insects in stored grain and many other stored commodities

Aluminium phosphide (AIP), a solid fumigant pesticide is widely used in India for grain preservation at homes and in warehouses

Aluminium phosphide (aluminum phosphide) is a highly toxic inorganic compound with the chemical formula AlP used as a wide band gap semiconductor and a fumigant. This colorless solid is generally sold as a grey-green-yellow powder due to the presence of impurities arising from hydrolysis and oxidation.

Properties



AlP crystals are dark grey to dark yellow in color and have a zincblende crystal structure with a lattice constant of 5.4510 Å at 300 K. They are thermodynamically stable up to 1,000 °C (1,830 °F).

Aluminium phosphide reacts with water or acids to release phosphine:

$AlP + 3\ H2O \rightarrow Al(OH)3 + PH3$ $AlP + 3\ H+ \rightarrow Al3+ + PH3$


ALUMINIUM PHOSPHIDE
CELPHOS®
FUMIGANT TABLETS

Preparation

AlP is synthesized by combination of the elements:

$4Al + P4 \rightarrow 4AlP$

Caution must be taken to avoid exposing the AlP to any sources of moisture, as this generates toxic phosphine gas.

Other names are Aluminum phosphide, Aluminium(III) phosphide, Aluminium mono phosphide ,Phostoxin, Fumitoxin.

Uses

Pesticide

AlP is used as a rodenticide, insecticide, and fumigant for stored cereal grains. It is used to kill small verminous mammals such as moles and rodents. The tablets or pellets, known as "wheat pills", typically also contain other chemicals that evolve ammonia which helps to reduce the potential for spontaneous ignition or explosion of the phosphine gas AlP is used as both a fumigant and an oral pesticide. As a rodenticide, aluminium phosphide pellets are provided as a mixture with food for consumption by the rodents. The acid in the digestive system of the rodent reacts with the phosphide to generate the toxic phosphine gas. Other pesticides similar to aluminium phosphide are zinc phosphide and calcium phosphide.

In this application, aluminium phosphide (Alp) is marketed in India under various trade names Alphos, Bidphos, Celphos,Fostox, Chemfume, Delicia, Fumigran, Phosphotek, Phosphume, Phostoxin, Quickphos, Synfume, Fumitoxin, Phostek , Phostoxin, Quick Phos, Talunex, Fieldphos, and Weevil-Cide. It generates phosphine gas according to the following hydrolysis equation.

Aluminium phosphide is said to be the most ideal grain preservative since it is relatively cheap while being very effective in repelling pests. The required number of tablets are removed from the airtight container and placed among the grain. On exposure to moisture, phosphine is released which percolates among the grain. When fumigated grains are subsequently well aerated, phosphine evaporates rapidly leaving behind virtually no residue. Traces of phosphite and hypophosphite of aluminium may be present, but they are non-toxic

$$2\ AlP + 6\ H2O \rightarrow Al2O3 \cdot 3\ H2O + 2\ PH3$$

It is used as a fumigant when other pesticide applications are impractical and when structures and installations are being treated, such as in ships, aircraft, and grain silos. All of these structures can be effectively sealed or enclosed in a gastight membrane, thereby containing and concentrating the phosphine fumes. Fumigants are also applied directly to rodent burrows.

Semiconductor applications

Industrially, AlP is a semiconductor material that is usually alloyed with other binary materials for applications in devices such as lightemitting diodes (e.g. aluminium gallium indium phosphide).

It is generally available as greyish green tablets of 3 grams each, mixed with urea and ammonium carbonate. These tablets are sold in sealed, airtight containers of tens and twenties. Each tablet liberates 1 gram of phosphine.

It protects the stored grain from pests, insects and rodents by liberating toxic phosphine (PH3) gas after coming in contact with moisture.

Each tablet/packet contains 56% of AIP and 44% of ammonium carbonate [(NH4)2 CO3] as active ingredients; is able to liberate PH3 by one-third of its weight. Phosphine, being a gas, diffuses uniformly throughout the grains and the residues such as phosphite and hypophosphite of aluminium are left in the packet/grains which are nontoxic.

The poisoning is generally suicidal, rarely homicidal and occasionally accidental (children) and is common in younger age groups.

MODE OF ACTION OF PHOSPHINE

Its toxic effects are due to the liberation of PH3 in the stomach after ingestion of AIP. Inhalation toxicity (inhalation of PH3) is uncommon and primarily involves lungs.

Fumigation has also caused unintentional deaths, such as examples in Saudi Arabia, and the United States Known as "rice tablet" in Iran, for its use to preserve rice, there have been frequent incidents of accidental or intentional death. There is a campaign by the Iranian Forensic Medicine Organization to stop its use as a pesticide.

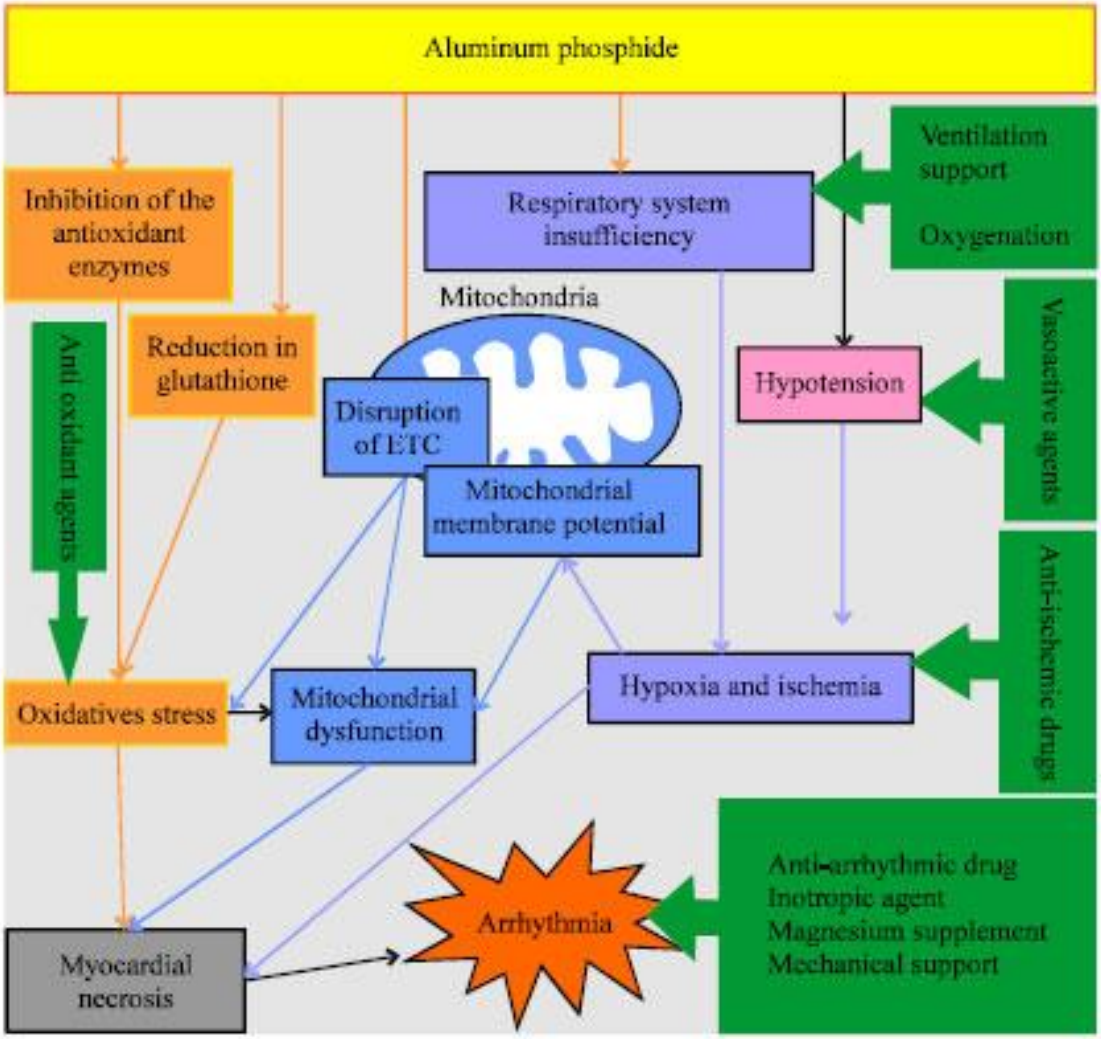
Recycling of used aluminium phosphide containers caused the death of three family members in Alcalá de Guadaira, Spain. They had been keeping them in plastic sacks in their bathroom. The deaths occurred accidentally due to aluminum phosphide reacting with water or moisture, and becoming phosphine, leading to their death within hours.

The other gases liberated in addition to PH3 include ammonia and CO2 which provide an inert media for PH3 to act:

$$AIP + 3HCI \rightarrow AICI3 + PH3\uparrow$$

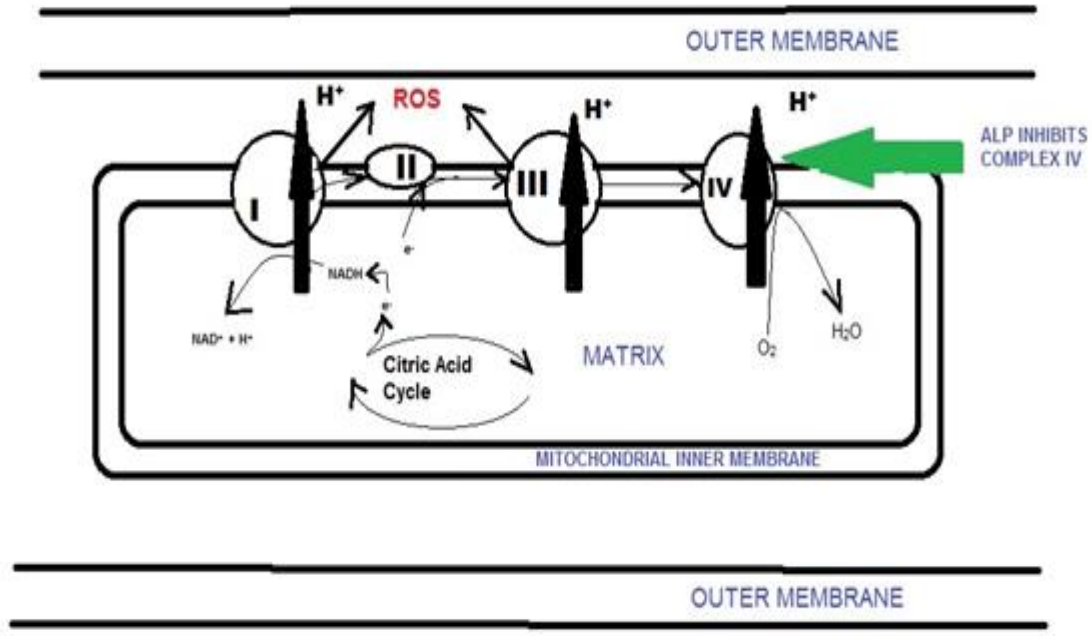
$$AIP + 3H2O\ (moisture) \rightarrow AI(OH)3 + PH3\uparrow$$

$$(NH4)2CO3 + H2O \rightarrow 2NH3\uparrow + CO2\uparrow + 2H2O$$


Aluminum phosphide
Inhibition of the antioxidant enzymes
Respiratory system insufficiency
Ventilation support
Oxygenation
Mitochondria
Anti oxidant agents
Reduction in glutathione
Disruption of ETC
Hypotension
Vasoactive agents
Mitochondrial membrane potential
Anti-ischemic drugs
Hypoxia and ischemia
Oxidatives stress
Mitochondrial dysfunction
Arrhythmia
Anti-arrhythmic drug
Inotropic agent
Magnesium supplement
Mechanical support
Myocardial necrosis

In one study Basic serum biochemical parameters, activity of mitochondrial complexes, antioxidant enzymes and parameters of oxidative stress were estimated in the platelets of patients who developed severe poisoning following ALP ingestion. These parameters were compared with healthy controls and with patients with shock due to other causes like cardiogenic shock, septic shock and hemorrhagic shock . The serum levels of creatine kinase-muscle brain and lactate dehydrogenase were higher in patients poisoned with ALP, whereas a significant decrease was observed in the activities of mitochondrial complexes I, II and IV. The activity of catalase was lower but the activities of superoxide dismutase and glutathione peroxidase were unaffected in them. A significant increase in lipid peroxidation and protein carbonylation was observed, whereas total blood thiol levels were lower. In patients severely poisoned with ALP, not only cytochrome c oxidase but also other complexes are involved in mitochondrial electron transport, and enzymes are also inhibited

The exact mode of action of PH3 is not known. It has been claimed to inhibit cytochrome c oxidase, a respiratory chain enzyme, similar to cyanide.

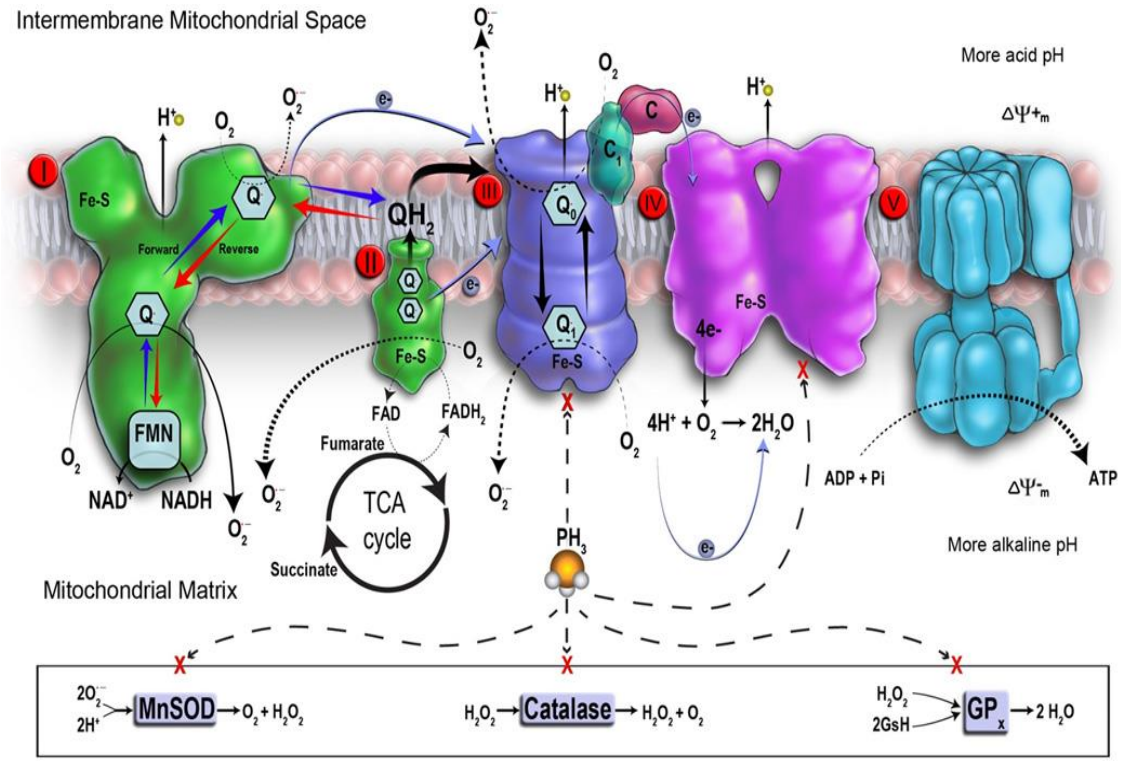


The effects of phosphine on electron transport and on some partial reactions of oxidative phosphorylation of mitochondria from mouse liver, housefly flight muscles and granary weevils has been studied. Phosphine was a strong inhibitor of respiration of mitochondria in the “active” state (state 3), uncoupled state, and ion-pumping state on glutamate, pyruvate plus malate, succinate, α-glycerophosphate, and ascorbate-cytochrome *c* as substrates. Respiration of mitochondria in state 3 was completely inhibited by about 250 μM phosphine. By contrast, the respiration of mitochondria in state 4 was much less sensitive.

This inhibition could not be released by uncouplers suggesting that it is due to a direct effect on electron transport. Only site III was inhibited to any significant extent. Kinetic studies show that the inhibition was noncompetitive with Ki ranging from 1.6×10^{-5} to 7.2×10^{-5} depending on

the source and purity of cytochrome oxidase. The inhibition of site III was also more pronounced in sonicated particles than in intact mitochrondria. The significance of this is discussed in relation to membrane sideness and topology of the components of the respiratory chain.

Phosphine was unable to activate the “latent” ATPase nor did it have any inhibition of the Mg^{2+}-simulated ATPase and only high levels (1.1 m*M*) showed modest inhibition (41%) of uncoupler-stimulated ATPase. Phosphine had no effect on the ATP-Pi exchange and on the ATP-ADP exchange reaction at concentrations causing strong respiratory inhibition.

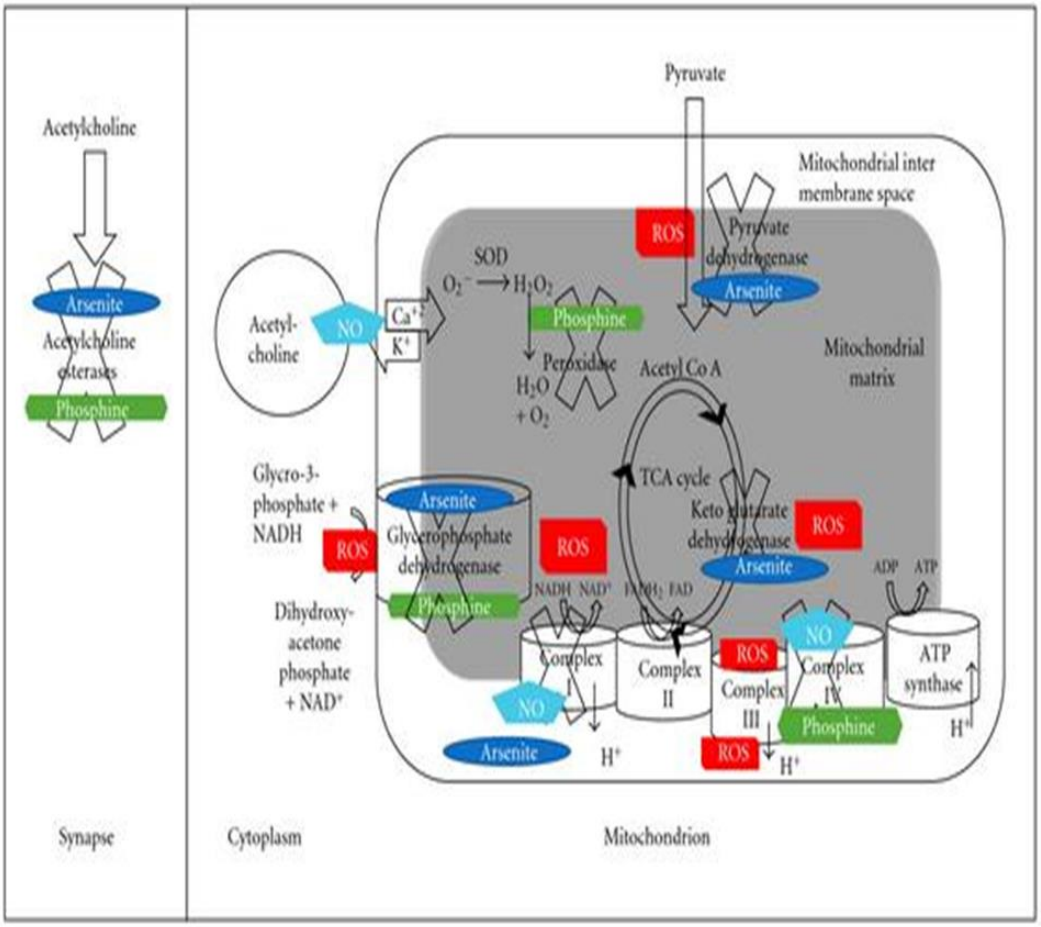


A schematic representation of the mitochondrial respiratory chain, ROS formation, and phosphine toxicity. The respiratory chain consists of specialized metal heme complexes such as complexes II, III, IV, and an ATP synthase known as complex V. Complex I, ubiquinone, cytochrome c, proton pumps, membrane potential, and proton motive force are critical parts of electron flow in the respiratory chain. Oxidative phosphorylation is carried out in the inner membrane by respiratory assemblies. From these assemblies, two electrons from NADH are transferred to O_2 by a series of electron carriers, starting with NADH dehydrogenase. Electrons are transferred to the ubiquinone (also known as coenzyme Q (CoQ)) and then to the cytochrome a group of hemeproteins. There are five cytochromes between CoQ and molecular O_2: cytochromes b, c1, c, a,

and a3. Cytochromes a and a3 are also known as cytochrome oxidase. The production of ATP occurs at 3 sites: (1) between NADH and CoQ, (2) between cytochromes b and c, and (3) between cytochrome c and O_2. The inner membrane is impermeable to most molecules because of its high proportion of phospholipids and cardiolipin. Transport proteins embedded in the inner membrane selectively incorporate metabolites into the matrix and export ATP for biological processes.

The matrix is the site of high energy–yielding reactions from the metabolism of pyruvate and fatty acids derived from carbohydrates and other nutrients. Pyruvate and fatty acids that are transported into the matrix help to generate a pair of electrons that have a high energy transfer potential. These are carried by NADH and FADH2 (flavin adenine dinucleotide reduced form), which are formed in glycolysis, fatty acid oxidation, and the citric acid cycle. The released high energy from this reaction is used to produce ATP through oxidative phosphorylation, which is a major metabolic reaction in aerobic organisms. Oxidative phosphorylation is strongly coupled to fatty acid oxidation, which forms acetyl CoA and the citric acid cycle to produce the energy needed for aerobic cell metabolism. Respiratory assemblies are an integral part of the inner membrane, whereas fatty acid oxidation and the citric acid cycle activity occur in the matrix. Flow of electrons causes an electrochemical proton gradient under the control of the proton motive force for the

production of ATP. During active respiration, mitochondria produce a proton motive force across the inner membrane. This results in a negative charge inside, thereby producing a pH gradient. Electron leakage from the respiratory chain from enhanced ROS production causes additional oxidative insult. If active electron flow ceases through the respiratory chain, proton motive force collapses and ATP production discontinues. This causes loss of membrane potential and release of additional ROS. The dashed arrows indicate the putative inhibition of critical components of the respiratory electron transport chain by phosphine.


Acetylcholine
Arsenite
Acetylcholine esterases
Phosphine
Synapse
Pyruvate
Mitochondrial inter membrane space
ROS
Pyruvate dehydrogenase
Arsenite
SOD
$O_2^- \rightarrow H_2O_2$
Phosphine
Acetyl-choline
NO
Ca^{+2}
K^+
Peroxidase
$H_2O + O_2$
Acetyl Co A
Mitochondrial matrix
TCA cycle
Glycro-3-phosphate + NADH
Arsenite
Glycerophosphate dehydrogenase
ROS
ROS
Keto glutarate dehydrogenase
ROS
Arsenite
ADP ATP
NADH NAD+ H_2O_2 FAD
Phosphine
Dihydroxy-acetone phosphate + NAD+
Complex I
Complex II
Complex III
Complex IV
ATP synthase
NO
ROS
NO
Phosphine
Arsenite
ROS
H^+
H^+
H^+
Cytoplasm
Mitochondrion

Interaction of phosphine with enzymes involved in metabolic processes and acetylcholine signalling.

Sites of interaction with arsenite and nitric oxide (NO) are also shown: phosphine (green), arsenite (dark blue), and nitric oxide (light blue).

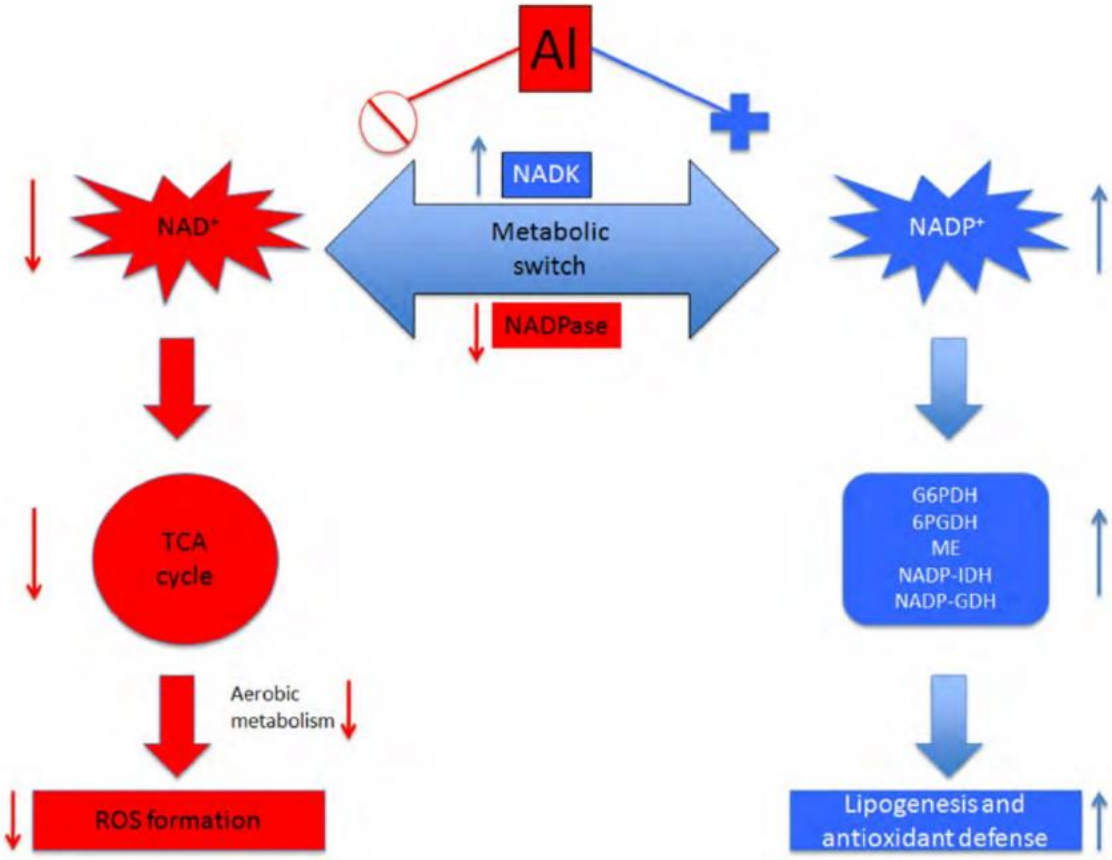
Sites of ROS generation (red) are indicated as well. The cross behind the names of targeted enzymes indicates that they are inhibited. The potassium and calcium currents are regulated by acetylcholine via NO. Ca^{2+} triggers the release of acetylcholine from vesicles in the cytoplasm into the neuronal synapse.

The acetylcholinesterase degrades acetylcholine, which reduces the strength of neurotransmission. The net effect is that arsenite and phosphine increase acetylcholine signalling by inhibiting the esterase.

FAD/FADH2 (Flavin adenine dinucleotide oxidised/reduced), NAD^{+}/NADH (nicotinamide adenine dinucleotide oxidised/reduced), ADP/ATP (adenosine di/tri nucleotide), NO (nitric oxide), ROS (reactive oxygen species), and TCA (tricarboxylic acid).

Some workers have claimed inhibition of mitochondrial catalase enzyme, extramitochondrial release of hydrogen peroxide (H2O2) and generation of oxygen free radicals by phosphine (PH3). Free radicals

seem to play a role in the initiation and propagation of cell damage, in addition to the direct toxic effects of phosphine.



Free radicals scavengers superoxide dismuatase (SOD) and catalase and lipid peroxidation were studied in patients of aluminium phosphide poisoning irrespective of age and sex admitted to a hospital in north India. Serial serum superoxide dismutase (SOD), catalase and MDA (malonyldialdehyde) were estimated on days 1, 2 and 5 post-admission depending on the survival of the patients. Serum SOD levels were significantly higher but serum catalase was significantly lower in patients than controls.On days 1 and 2 which suggested stimulation of SOD and inhibition of catalase by phosphine resulting in excessive

hydrogen peroxide (H2O2) load. Significantly higher levels of MDA in patients than controls on days 1 and 2 indicated enhanced lipid peroxidation in this poisoning. The significantly high levels of SOD and MDA in non-survivors suggested their direct relation to mortality while catalase levels had an inverse relationship. Return of SOD and catalase and MDA to normal or near normal levels in survivors by day 5 suggested abolition of an oxidative stress due to elimination of phosphine.

Most of the toxic effects of metal phosphides are owed to PH3, which is a protoplasmic poison that interferes with the function of the cellular enzymes and proteins. According to some authors, the mechanism of its toxicity is electron transfer blockage and non-competitive blockage of cytochrome C oxidase, which inhibits oxidative phosphorylation and, in turn, cellular respiration and activation of peroxide radicals.

Phosphine can inhibit catalase and deplete glutathione, which may result in cellular wall and canal dysfunction as well. According to Proudfoot, studies have shown that phosphine impairs cellular respiration. It inhibits the entrance of amino acids into the cycle of myocardial protein synthesis and also inhibits cytochrome C oxidase in cardiac cells. According to Anand et al, these changes in the mitochondria and

myocardial proteins impair cellular permeability to sodium, potassium, magnesium, calcium, and other ions and change cardiac cell wall potential.

Phosphine-induced pathophysiological changes are more prominent in the myocardium, pulmonary cells, and tiny peripheral vessels. Both AlP and phosphine inhibit cholinesterase, but this inhibition is unlikely to be clinically relevant. Another toxic action of phosphine is that it changes the capacity of haeme. In vitro studies show that humans and rats can absorb unhydrolysed aluminium phosphide salt, which keeps reacting with free haemoglobin and haemoglobin in normal red blood cells (RBCs) to produce haemichrome, a derivative of methaemoglobin. Levels of carbon monoxide, which can be established by CO-oximetry, can help diagnosis and prognosis of AlP poisoning. Namely, phosphine may affect oxyhaemoglobin that interacts with CO and cause dyshaemoglobinemia, which can yield high CO findings. Considering that phosphine produces free oxygen radicals in body tissues, it has been shown that organs with a higher need for oxygen (heart, lung, kidney, and liver) are more sensitive to the damage induced by phosphine gas, which is compatible with the post-mortem histopathological changes in these organs. In addition, Heinz bodies, which are indicative of the destruction of haemoglobin in vitro, increase to 1.25 μg mL-1 in poisoned patients.

Occupational and environmental phosphine exposure Occupational exposures to phosphine are uncommon and rarely severe (Sudakin, 2005) but accidental inhalation is a particular risk to those in close proximity to grain that has had a metal phosphide mixed in with it.

Recurring locations include ships holds (Gregorakos, et al, 2002, Hansen & Pedersen, 2001, Vohra, et al, 2006), Rail wagons (Perotta, et al 1994, Vohra, et al, 2006), Grain elevators (Abder-Rahman, et al, 2000), Grain stores (Brautbar & Howard, 2002, Misra, et al, 1988), and even stores in homes (Abder-Rahman, et al, 2000).

Potentially lethal concentrations of the gas may develop in the head-spaces of unventilated or poorly ventilated storage containers and domestic premises (Memis, et al, 2007).

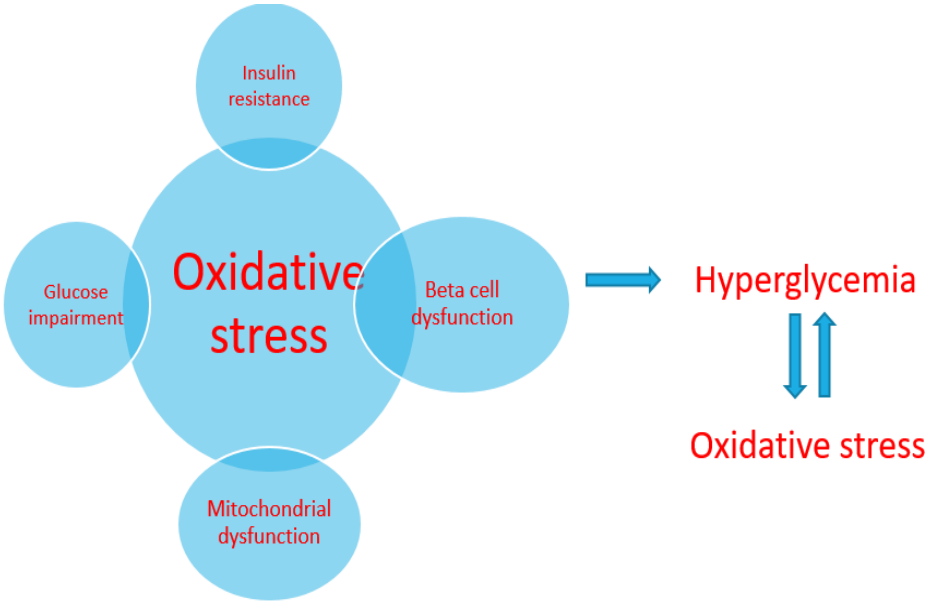
Phosphine may be released during the illicit manufacture of methamphetamine (Burgess, 2001, Willers-Russo,1999); deaths have resulted (Willers-Russo, 1999).

In another incident, a packet of aluminium phosphide in a container from abroad burst open and the sweepings placed in water causing immediate fizzing and liberation of phosphine (Kamanyire & Murray, 2003).

Close proximity to a source of phosphine is not required to be at risk of toxicity as phosphine gas can travel some distance as it is heavier

than air (vapor density 1.2:1). Many years ago 12 individuals in a house adjacent to a warehouse used to store aluminium phosphide developed vomiting and one died. The illnesses were attributed to phosphine (Glass, 1959).

More recently exposures have been alleged after use of metal phosphides to control pests in adjacent buildings



- The above mechanisms may explain the fact that hyperglycemia is a poor prognostic factor in aluminium phosphide poisoning.
- The administration of Hyperinsulinemia euglycemia therapy has an advantage in improving mortality in AlP posoining.
- It improves inotropy and peripheral vascular resistance and reverse acidosis by improving myocyte carbohydrate uptakeand utilisation.
- Thus, oxidative stress can be possibly ameliorated by management of hyperglycemia and changes or disruptions in these mechanisms may reduce the risk of insulin resistance and the development of hyperglycemia and, furthermore, may have a potential role in its treatment

CLINICAL TOXICITY

Forensic Issues Prior to 1980, aluminium phosphide poisoning was virtually unreported in India. Today it is the leading cause of suicidal (and sometimes accidental) death in northern Indian states such as Punjab, Haryana, Uttar Pradesh, Madhya Pradesh, and Rajasthan. Southern states have so far not been significantly affected since aluminium phosphide is yet to make inroads into the agricultural sector here. But there are ominous indications of a gradual rise in the number of cases being reported

The toxic dose of oral AIP compound is 500 mg/70 kg in humans. Toxicity occurs either due to suicidal ingestion of AIP or inhalation of liberated PH3 from fumigated grains. The lethal dose of AlP in a normal 70-kg adult has been reported to be 500 mg. In the work place, air phosphine level of 50 mg L-1 (50 ppm) may be dangerous for health, and 400-600 mg L-1 (400-600 ppm) may cause death in 30 minutes.

Lethal dose or concentration (LD, LC): LD50 (median dose) 11.5 mg/kg.

Phosphine is widely absorbed and distributed in the tissues. It is also known that AIP is absorbed as such and possibly deposited in liver leading to slow release of PH3 which may be responsible for extended poisoning in humans.

The signs and symptoms of acute, moderate-to-severe ingestional poisoning appear within 45 minutes to one hour. The organs involved include gastrointestinal tract, heart, lungs, liver, kidneys and the brain.

Inhalational toxicity is invariably accidental; occurs in persons sleeping in warehouses where stored grains are fumigated with AIP.

An exposure to high PH3 concentration leads to shock or cardiovascular collapse but a lower concentration produces pulmonary oedema.

However, the lower concentration (7.5 mg/m3) may cause cough, dyspnoea and mild respiratory failure.

CLINICAL FEATURES

Aluminium phosphate poisoning affects the most organs and a variety of signs and symptoms appear in patients. Early symptoms include nausea, vomiting, retrosternal and epigastric pain, dyspnea, anxious, agitation and smell of garlic on the breath.

Moreover shock and peripheral circulatory failure are mainly imperative early signs of toxicity. Mortalities in past studies have ranged from 40–77% and in one survey 55% occurred within 12 h of ingestion and 91% within 24 h.

CARDIAC TOXICITY

Cardiac toxicity comprises circulatory failure ,hypotension, congestion of the heart, separation of myocardial fibres by edema, fragmentation of fibres, non-specifc vacuolation of myocytes, focal necrosis, neutrophil and eosinophil infiltration were found in autopsy . Also, significantly increasing left ventricular dimensions , hypokinesia of the left ventricle and septum, akinesia, ejection fractions reduction , severe hypotension, raised systemic venous pressure, normal pulmonary artery wedge pressure, inadequate systemic vasoconstriction and ECG abnormalities are sinus tachycardia, sinus arrhythmia with ST segment depression in lead II, III, and AVF, ST elevation, atrial fibrillation, T wave inversion in V5-6, sinus arrest, chaotic atrial pacemaker, complete heart block, bundle branch block, and ventricular premature complexes followed by ventricular tachycardia. Massive focal myocardial injury with elev ated serum levels of cardiac enzymes may occur.

RESPIROTORY TOXICITY

Tachypnea, dyspnea, crepitations, and rhonchi were present on examination of phosphide poisoning. Respiratory distress is invariably present with cyanosis, and cold, clammy skin. Pulmonary edema is common but it is not always clear whether it is cardiogenic or non-cardiogenic in etiology. It tends to develop 4–48 h after ingestion and the finding of a reduced arterial pressure of O2 without an increase in pulmonary artery wedge pressure, suggested it was non-cardiogenic. Others have confidently diagnosed adult respiratory distress syndrome and non-specific pulmonary edema and the edema fluid may be protein-rich and hemorrhagic.Type 1 and Type 2 respiratory failure may occur.

GASTROINTESTINAL TOXICITY

Hematemesis , corrosive lesions of the esophagus and stomach , vomiting, epigastric pain, severe gastric erosions, duodenal erosions, esophageal strictures tracheo-oesophageal fistulae,dysphagia. Dysphagia may be apparent as soon as 3 or 4 days after ingestion of aluminium phosphide but is more usual about 2 weeks later.

In some rare presentations diarrhoea may occur.

HEPATIC TOXICITY

Transient elevations of alanine aminotransferase and aspartate aminotransferase activities are not infrequent after ingestion of metal phosphides) but jaundice secondary to liver damage is much less common. Jaundice was alleged to be present in members of the crew of a grain freighter who inhaled phosphine after an accidental release.Serum bilirubin concentrations were normal and transaminase activities only minimally disturbed. Acute hepatic failure and encephalopathy was considered to be the cause of death insome patients. a 12-yearold girl died from a combination of acute hepatic failure and encephalopathy with renal failure shows in the study of Bayazit, et al. Portal edema, congestion of the portal tract and central veins, and vacuolization of hepatocytes are the most frequent findings at autopsy.

ELECTROLYTE AND METABOLIC ABNORMALITIES

Hypokalemia, metabolic acidosis, mixed metabolic acidosis and respiratory alkalosis, and acute renal failure are reported frequently. Also,hyperglycemia and Hypoglycemia and hypomagnesemia have been reported in several studies.

Hypokalemia is common soon after ingestion of metal phosphides and is probably secondary to vomiting, though catecholamine release could also contribute. It is thought to be the result of impaired gluconeogenesis and glycogenolysis possibly secondary to adrenal gland damage and low circulating cortisol concentrations. Hyperglycemia reported in study of Abder-Rahman, 1999 and it appears to be rare. The main controversy relates to the existence or otherwise of disturbances of magnesium homeostasis. In 1989, prompted by reports of the empirical use of magnesium sulphate to treat phosphide toxicity, this study demonstrated that serum magnesium concentrations were increased, possibly secondary to release from damaged cardiac myocytes and hepatocytes, and confirmed the findings in subsequent studies. Unfortunately, other studies have found the converse, that is serum and erythrocyte concentrations were reduced rather than increased. Compared serial serum and erythrocyte magnesium concentrations in four groups of people. One comprised patients poisoned with aluminium phosphide who

had resulting shock and cardiotoxicity while the second included those poisoned but without shock or cardiac features. The remaining two groups acted as controls, the first being patients in shock secondary to trauma or hemorrhage but without other features of cardiac toxicity and the second, normal volunteers. The only significant finding in admission samples was that cell and serum concentrations were lower in shocked, cardiotoxic patients.

Hypomagnesemia was found in toxic shocked patients but not in those with non-toxic shock and secondly, 75% of those in the toxic/shock group had ECG changes, it was concluded that the evidence supported a causal relationship between hypomagnesemia and phosphide induced shock. Without intervention both serum and cell values returned to normal by about 24 h,and thought the hypomagnesemia secondary to consumption in combating free radical stress. Hypomagnesemia has also been found in a recent single case of phosphine inhalation from aluminium phosphide. They found pre-treatment mean serum and red cell magnesium concentrations to be normal. Concentrations were increased in the brains, lungs, hearts, livers, kidneys, and stomachs of fatalities but later studies showed this to be the result of magnesium administration and not phosphide toxicity. Clearly, these studies cannot all be correct and the analytical method used to generate the results may be an important factor. The results of a study (Siwach, et al, 1994) carry particular weight

because they used atomic absorption spectroscopy, a technique that is superior to the colorimetric method published in 1977 and used and the titan yellow method employed. Eventhough the results obtained using the former method correlated extremely well with those from atomic absorption spectroscopy there is no choice but to accept that neither hypomagnesemia nor hypermagnesemia is a feature of aluminium phosphide poisoning.

HEMATOLOGICAL TOXICITY

Although phosphine causes Heinz body formulation and hemoglobin oxidation in vitro, intravascular hemolysis and methemoglobinaemia are unusual complications of phosphide poisoning in humans. Nine patients with intravascular hemolysis after ingestion of aluminium phosphide have been identified from the pervious studies.

Glucose-6-phosphate dehydrogenase deficient, including one young man who had previously developed haemolysis when given primaquine. Intravascular hemolysis was associated with renal failure and severe metabolic acidosis to which 3 days of vomiting and diarrhea may have partly contributed. In addition to hemolysis some patients found to have methemoglobinaemia of 17% 32 h post-ingestion while another developed Heinz bodies, a further indicator of damage to hemoglobin.

Rats given aluminium phosphide had methemoglobin concentrations measured at 10 and 30 min intervals. They increased simultaneously with those of malonyldialdehyde suggesting that methemoglobinaemia was secondary to increased oxygen free radical generation.

A study revealed that there is a significant association between blood level of methemoglobin and mortality in patients with aluminium phosphide intoxication.

Disseminated intravascular coagulation was present patients poisoned with aluminium phosphide.

UNCOMMON FEATURES

Unusual complications of phosphide ingestion include atrial infarction,Bleeding diathesis, adrenocortical congestion, hemorrhage and necrosis, pancreatitis, and renal failure. Acute pericarditis has also been reported infrequently though pericardial fluid was detected by echocardiography in a patients in one study. Subendocardial infarction complicated the recovery of a 16-year-old male and a 26-year-old woman who had recovered from aluminium phosphide ingestion reported in some studies. Some patients suffered an intracranial hemorrhage 5 days after the event. No explanation other than the poison was found in that patient. Convulsions have been reported in some cases. Coma supervenes in later stages.

INVESTIGATIONS

1. Blood sugar value at the time of admission
2. Complete haemogram
3. Blood biochemistry, e.g. urea, sugar, creatinine, transaminases, bilirubin, electrolytes, etc.
4. Electrocardiogram (ECG) for arrhythmias, myocarditis and conduction defects.
5. Chest radiograph (posteroanterior view) for acute respiratory distress syndrome (ARDS), aspiration pneumonia, etc.
6. Blood gas analysis for hypoxia and acidosis
7. Serum magnesium levels
8. Toxicologic screening, e.g. blood phosphine levels.

DIAGNOSIS

1. Garlicky odour in the breath.
2. Urinalysis may reveal occult blood, bilirubin, glucose, and albumin.
3. Liver function tests are often abnormal.
4. Blood urea and serum creatinine are usually higher than normal.
5. Hypo/hypermagnesaemia; hypo/hyperphosphataemia.
6. ECG changes (mentioned under Clinical Features).

Qualitative tests for detecting phosphine in the breath and gastric aspirate:

a. Breath test: A piece of filter paper impregnated with 0.1 N silver nitrate solution is used in the form of a mask through which the patient is asked to breathe in and out for 5 to 10 minutes. Blackening of the paper is indicative of the presence of phosphine in the breath, since silver nitrate is reduced to silver on exposure to it. Similar reaction is also produced by hydrogen sulfide.

b. Biological sample test: A small amount of gastric apirate (5 to 10 ml) or minced tissue (5 to 10 gm of liver)* is taken into a steam distillation flask to which an equal quantity of water is added and then acidified with dilute HCl or H2SO4, followed by heating upto 500C for 15 minutes. The distillate is collected in an ice cold

receiver containing 5 ml of 1% silver nitrate solution by dipping the adapter into it. If phosphine is present, the solution will turn black.

i. For confirmation, add 5 ml of concentrate.HNO3 to the black precipitate and boil till the solution becomes clear. Then add 5 ml of ammonium molybdate solution and heat for a minute. Formation of a yellow precipitate confirms the presence of phosphine.

ii. A variation of this test involves placing 0.1 N lead acetate filter paper over the mouth of the distillation flask containing the sample (prepared in the same manner as detailed above). The flask is heated for 15 minutes at 50oC. Phosphine will blacken the silver nitrate paper, while hydrogen sulfide will blacken both papers.

Nil toxicity means ingestion of exposed compound (tablets kept out of containers or powder in open packets) which does not produce any systemic manifestation except local symptoms such as nausea, vomiting or retrosternal burning. Prognosis is excellent.

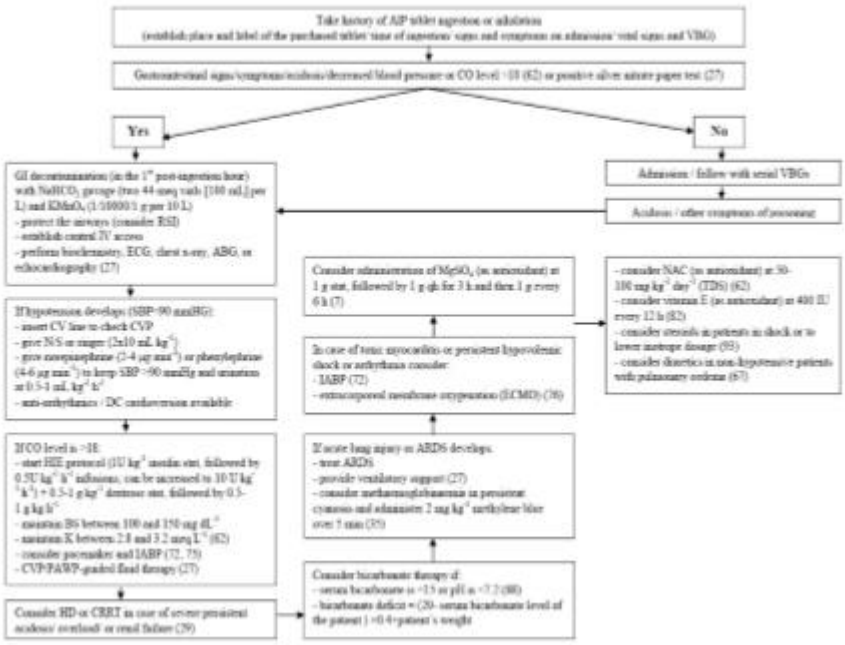
Mild ingestional toxicity is diagnosed by the history of taking a small dose of partially exposed compound (broken tablet/ exposed packet/non-smelling tablet). There is a slight drop in blood pressure with nausea, vomiting, retrosternal burning or pain. Arrhythmias are occasional and metabolic acidosis is rare. AgNO3 test is negative. Most of these patients survive.

All types of cardiac arrhythmias (brady- or tachy-arrhythmias) have been observed either alone or in combination with other ECG changes in 40% to 80% patients with moderate-to-severe poisoning. The ST segment elevation/depression due to acute myocarditis is also observed commonly (30%). The conduction disturbances (sinoatrial, atrio-ventricular, bundle branch blocks, intra-ventricular conduction delay, etc) are least common, occurring in 5% to 10% patients.

There may be hypoxaemia (PaO2 <60 mmHg) and metabolic acidosis (pH <7.1) in 75% to 80% cases. Magnesium levels have been found to be low or normal. Hypokalaemia,hyperlycemia or hypoglycaemia has been observed.

Sometimes, patients may not divulge the history of AIP ingestion. In such a situation, a high degree of suspicion combined with sudden onset of unexplained shock or cardiac arrhythmias and blood samples, if appear too dark to explain, form important clues to the diagnosis of this poisoning in younger patients.

MANAGEMENT



The early recognition and management is essential to reduce mortality.

The main goal of therapy is to sustain life till PH3 gets excreted. Steps to Remove as well as to Retard PH3 Absorption.

DECONTAMINATION

Gastric lavage is probably best avoided after ingestion of phosphides as it might increase the rate of disintegration of the pesticide and increase toxicity. To reduce the absorption of phosphine, gastric lavage with potassium permanganate (1:10,000) is done. Permanganate is used as it oxidizes PH3 to form non-toxic phosphate. This is followed by a slurry of activated charcoal (approximately 100 gm) given through a nasogastric tube. In vitro studies suggested that vegetable oil and liquid paraffin inhibit phosphine release from phosphides but these oils have not been tested in clinical practice. However, vomiting may make the administration of charcoal difficult. Although the administration of sodium bicarbonate via a gastric tube to decrease gastric hydrochloric acid has been proposed in the belief that hydrochloric acid assists the conversion of phosphide to phosphine, there is no experimental support for its use. Moreover, based on an understanding of the mechanisms of toxicity of metal phosphides, this strategy is unlikely to reduce morbidity and mortality. Removal of victims of phosphine inhalation from the contaminated atmosphere will have been carried out by the emergency service first on scene. Supplemental oxygen may be given if necessary but further measures for airway control are unlikely to be required

Judicious use of antacids (60 mL/hour) to reduce gastric symptoms and to reduce PH3 absorption. In addition, if needed H2-blockers may be given as intravenous infusions.

STEPS TO REDUCE TISSUE TOXICITY

There is no specific antidote to phosphine.

Magnesium sulphate possesses membrane stablising properties and has been used in several studies from India.

The effective dose schedule is to start with 1 g IV, then 1 g IV after one hour for 3 consecutive hours, then 1 g IV infusion after 4 to 6 hours for 3 to 5 days. It can reverse some arrhythmias and mortality is reduced.

Phosphine is a stable, partially water soluble gas and is excreted to some extent in the urine but is mainly excreted through breath; hence, adequate hydration and renal perfusion by IV fluids and low-dose dopamine 2 to 4 μg/kg/min must be maintained to allow its renal excretion.

Diuretics are not useful in the presence of shock. Patients with severe poisoning are haemodynamically unstable but maintain a good urine output, hence, dialysis is usually not done. If acute renal failure develops and patient is haemodynamically stable, then dialysis may be useful.

SUPPORTIVE MEASURES

Many patients will die from metal phosphide poisoning despite intensive care. Supportive measures are all that can be offered and should be implemented as required by clinical developments. The most important factor for success is resuscitation of shock and institution of supportive measures as soon as possible. Intravenous access should be established and 23 litres of normal saline are administered within the first 8-12 hr guided by central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP). The aim is to keep the CVP at around 12-14 cm of water Some workers have recommended rapid infusion of saline (3-6 litres) in the initial 3 hr .

Low dose dopamine (4-6 μg/kg/min) is given to keep systolic blood pressure >90 mm Hg. The other vasopressures such as norepinephrine may be usefull in critical patients. The use of high doses of glucagon may benefit in the treatment of aluminum phosphide poisoning; the likely mechanism of action is the increase of cAMP in the myocardium, effectively bypassing the β-adrenergic second messenger system. Oxygen is given for hypoxia. Acute respiratory distress syndrom requires intensive care monitoring and mechanical ventilation.

The blood glucose concentration should be measured in every case and hypoglycemia corrected if found. Similarly, hypokalemia should be

sought and, if clinically indicated, at least partially corrected; cardiac features have resolved in occasional patients on correction of potassium concentrations. It must be remembered, however, that the onset of acidosis, renal failure and cell damage may produce life-threatening hyperkalemia. Metabolic acidosis should be managed conventionally. Bicarbonate level less than 15 mEq/L requires bicarbonate in a dose of 50-100 mEq intravenously every 8 hour

ECMO indications and procedure

VA ECMO was considered for patients with AlP poisoning who were classified as high-risk group as defined below.

The patients of AlP poisoning were classified as a high risk if they met the following criteria:

1. Left ventricular myocardial dysfunction i.e. EF of ≤35%
2. Severe metabolic acidosis (pH ≤ 7.0) and/or refractory shock i.e. systolic blood pressure <80 mmHg despite conventional medical therapies.

The cannulation site was determined based on patient status. The majority of patients underwent percutaneous cannulation through femoral vessels. The ECMO cannulation was done in intensive care unit. A venous cannula was placed in the inferior vena cava or right atrium for drainage infusion. The usual size of venous cannula ranges from 21 to 25 F. The return cannula is a short arterial cannula inserted via the common femoral artery. This cannula is fully inserted to the taper, with the tip lying in the common iliac artery or lower aorta. The usual size of arterial cannula ranges from 17 to 21 F. Additional distal perfusion 9 F return cannula (“backflow cannula”) is inserted antegradely into the common femoral artery and directed into the superficial femoral artery.

The patients were maintained on a continuous heparin infusion to achieve an activated clotting time between 180 and 200 s.

The goal for the activated clotting time was adjusted if there were issues with bleeding or coagulation. To maintain a hemoglobin level of ≥10 g/dL and a platelet count of ≥100,000 dL^{-1}, patients received a transfusion during the ECMO treatment.

The patients were continuously monitored in terms of hemodynamic improvement, reversal of metabolic acidosis, and adequate oxygenation. Once these parameters are satisfactory, the ECMO weaning protocols were initiated. The circuit flow was reduced to assess the native cardiac function in the setting of an increased venous return. Flow was reduced from 2.5 L/min in a series of 0.5 L/min increments while hemodynamic and echocardiographic evaluations were done.

Decannulation was performed once the patient had improvement in LVEF to >35%, maintaining systolic blood pressure of >90 mmHg without any inotropic support and acidosis had recovered.

Venoarterial ECMO has shown promising improvement in the short-term survival of adults with AlP poisoning associated with LV dysfunction and severe metabolic acidosis and/or refractory shock.

However, ECMO is also associated with significant complication rates. Another important highlight is the early presentation to the hospital

and immediate referral to the tertiary care center with facility and experience to use ECMO. The decision to start ECMO should be prompt.

TREATMENT OF COMPLICATIONS

1) Hypoxia

O2 inhalation, patent airway (endotracheal intubation and assisted ventilation, if necessary). Monitor blood gases.

2) Shock

Intravenous (IV) fluids (2 to 3 litres, out of which 50% should be saline) to be given during first 3 to 6 hours guided by central venous pressure or pulmonary capillary wedge pressure. Monitor electrolytes. Blood pressures should be monitored and kept above 80 mm Hg. Low-dose of dopamine (2 to 4 µg/kg/min) and dobutamine (2.5 to 5 µg/kg/min) may be used in combination to maintain renal perfusion. IV hydrocortisone (200 to 400 mg) every 4 to 6 hours has been used to restore sensitivity to endogenous catecholamines.

3) Arrhythmias

Conventional antiarrhythmic drugs such as digoxin and xylocaine are ineffective. Others drugs being myocardial depressants are avoided but amiodarone has been used to combat fatal arrhythmias. Atropine has been found ineffective in bradyarrhythmias.

MgSO4 has also been found effective as a potent antiarrhythmic drug in the presence of hypoxia (anti-hypoxic effect), has been extensively used and found to be effective in certain arrhythmias.

4) Metabolic acidosis

IV sodium bicarbonate to keep the HCO3– levels around 18 to 20 mmol/L and pH >7.1. Dialysis is to be done if metabolic acidosis persists and patient is haemodynamically stable.

5) Acute respiratory distress

Remove the patient to open air and loosen the clothes around the neck. To achieve PaO2 around 60% with distress syndrome lowest inspired fraction of O2 (FiO2), oxygen is delivered by simple face mask or face mask fitted with inspiratory (ARDS)/noncardiogenic reservoir bags at moderate flow rates (5 to 10 L/min of 100% O2).

Mechanical support is indicated if above pulmonary oedema measures fail. Positive end expiratory pressure therapy may be tried to lower FiO2 below 0.6 provided patient is haemodynamically stable.

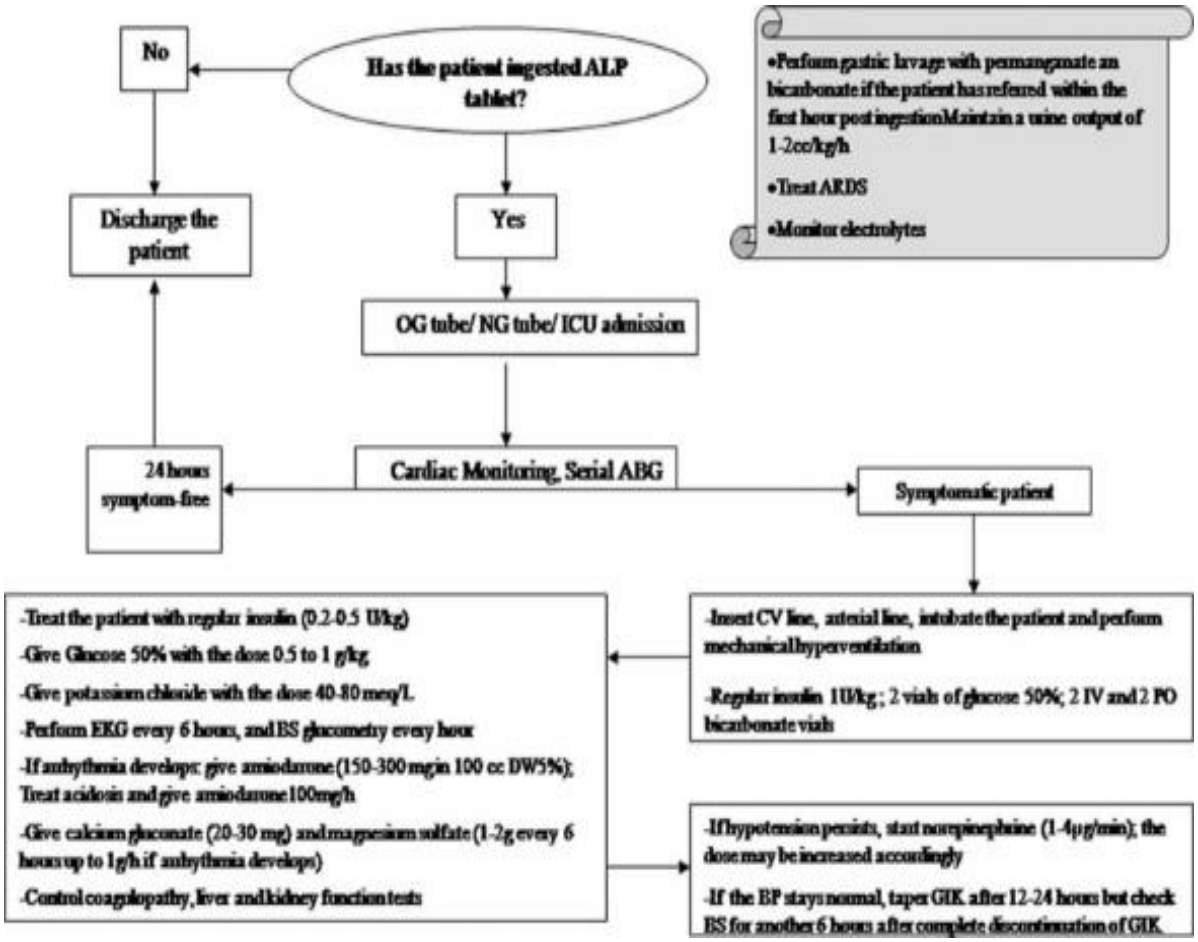
Swan-Ganz catheter may be inserted for monitoring arterial and pulmonary wedge pressure, to measure cardiac output, fluid therapy, to monitor blood gas analysis and to guide diuretic therapy.

6) Hypoglycaemia

IV dextrose to combat hypoglycaemia which is reversible.

7) Hyperglycemia

Treated with insulin along with other supportive measures to achive desired goal.



Presently the suggested measures include the following:

a. Management of circulatory shock with IV fluids (4 to 6 L over 6 hours), while monitoring the central venous pressure and/or pulmonary wedge pressure. Dopamine can be given IV at a dose of 4 to 6 mcg/kg/min (maximum 10 mcg/kg/min).

b. Management of respiratory distress with 100% humidified oxygen, intubation, and assisted ventilation.

c. Management of metabolic acidosis with sodium bicarbonate (50 mEq/15 min) until the arterial bicarbonate rises above 15 mmol/L.

d. Control of convulsions with anticonvulsants (benzodaizepines, barbiturates, etc.).

e. Magnesium sulfate therapy*: Magnesium sulfate is said to be beneficial in the management of cardiac arrhythmias. Conventional antiarrhythmic drugs such as digoxin and lidocaine are ineffective.

i. Magnesium sulfate is given IV as a 3 grams bolus, followed by 6 grams infusion over 24 hours for 5 to 7 days.

ii. Alternatively, 1 gram can be given IV to begin with, followed each hour by the same dose for 3 consecutive hours, and then 1 gram every 6 hours for 5 days.

4. Ranitidine 50 mg IV 8th hourly to counter the severe epigastric pain.

MORTALITY

Mortality is highly variable (37% to 100%) depending on the factors such as dose of the fresh pesticide consumed, early vomiting, duration and severity of poisoning, severity of shock and its response to resuscitative measures, etc. The most common cause of death is acute cardiovascular collapse followed by the development of ARDS. Early vomiting is the single factor that improves mortality.

POSTMORTEM FINDINGS

Postmortem findings include the viscerae to be heavy, oedematous and emitting foul smell.

The lungs show desquamated epithelium with alveoli thickened by haemolysed red blood cells and leucocytic infiltration around bronchioles

The liver shows congestion, oedema, areas of centrizonal necrosis and mild-to-moderate fatty infiltration.

The heart shows congestion, oedema, fragmented fibres, focal areas of myocardial necrosis and leucocytic infiltration.

The kidneys show congestion, oedema, necrosis and degenerative and regenerative activity of the tubules.

The stomach and the intestines also show congestion, oedema and leucocytic infiltration with sloughing of mucosa.

OBJECTIVES

1. To study the blood glucose levels in aluminium phosphide poisoning
2. To evaluate the role of hyperglycemia as a potential prognostic factor in acute aluminium phosphide poisoning

SOURCE OY DATA

The study will be conducted on 40 patients admitted in Government Rajaji Hospital & Madurai Medical College during the study period from april 2017 to august 2017.

INCLUSION CRITERIA

40 consecutive patients admitted with aluminium Phosphide Poisoning

EXCLUSION CRITERIA

Known case of Diabetes Mellitus

DATA COLLECTION

Informed consent will be obtained from all patients to be enrolled for the study. In all the patients relevant information will be collected in a predesigned proforma.

The patients are selected based on clinical examinations, biochemical tests and History of aluminium Phosphide Poisoning.

Patients were subjected to routine Investigations and Random Blood Sugar At the Time of admission.

LABORATORY INVESTIGATIONS

a) Complete blood count,

b) Liver function test,

c) Renal function test,

d) Urine routine,

e) blood sugar on admission

DESIGN OF STUDY

Prospective study.

PERIOD OF STUDY

6 MONTHS (may 2017 to august 2017)

COLLABORATING DEPARTMENT

DEPARTMENT OF BIOCHEMISTRY

ETHICAL COMITTIE CLEARENCE : clearance applied

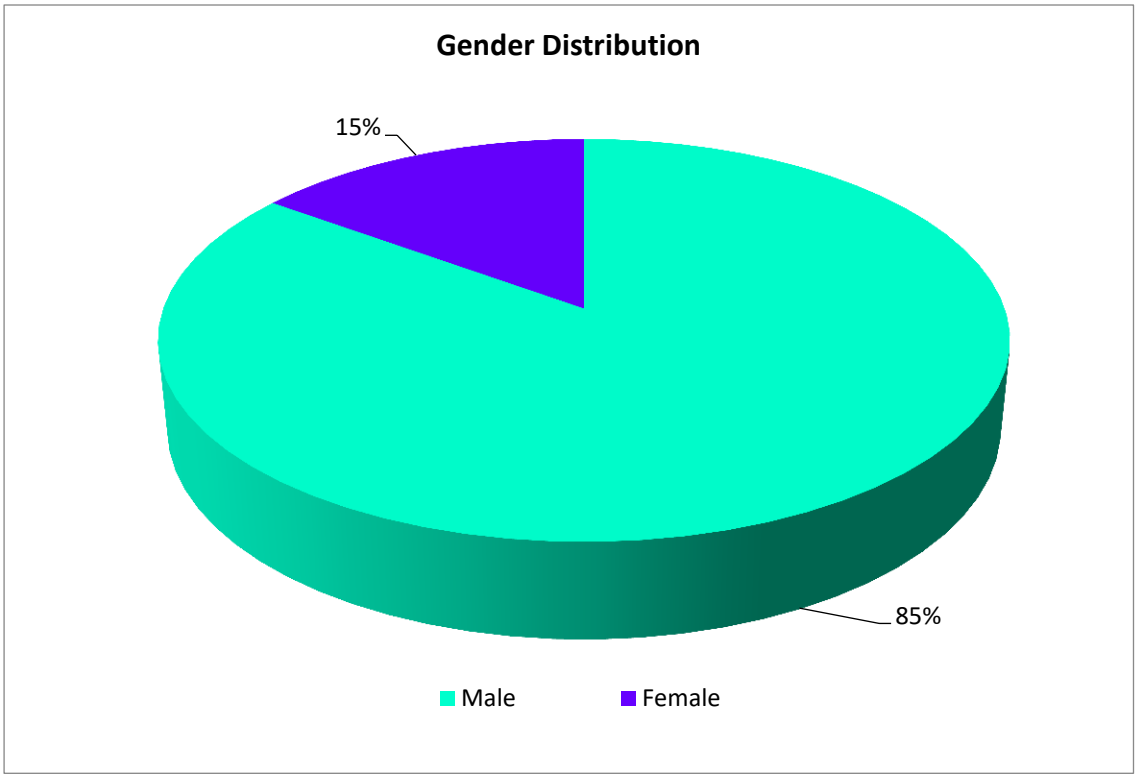
CONSENT**:** Individual written and informed consent

ANALYSIS: Statistical analysis

CONFLICT OF INTEREST: Nil

FINANCIAL SUPPORT: Self

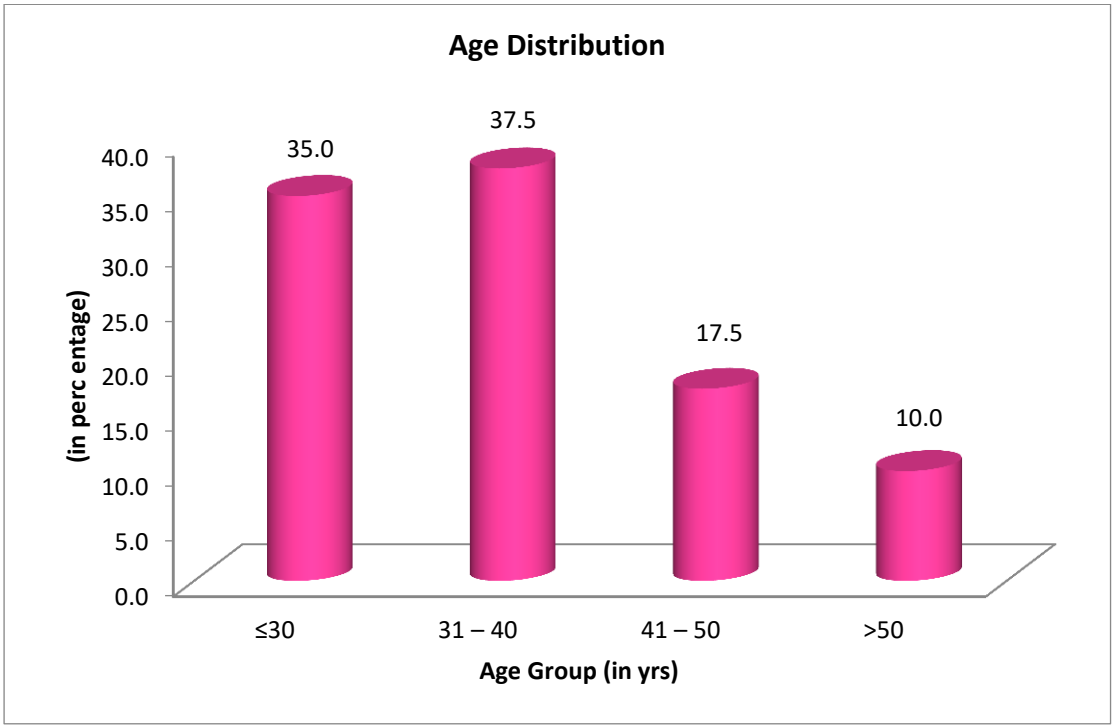
RESULTS



Gender	No. (%)
Male	34 (85.0)
Female	6 (15.0)
Total	40 (100.0)

COMMENTS

Among 40 patients, 34 were male patients and 6 were female patients in this study.

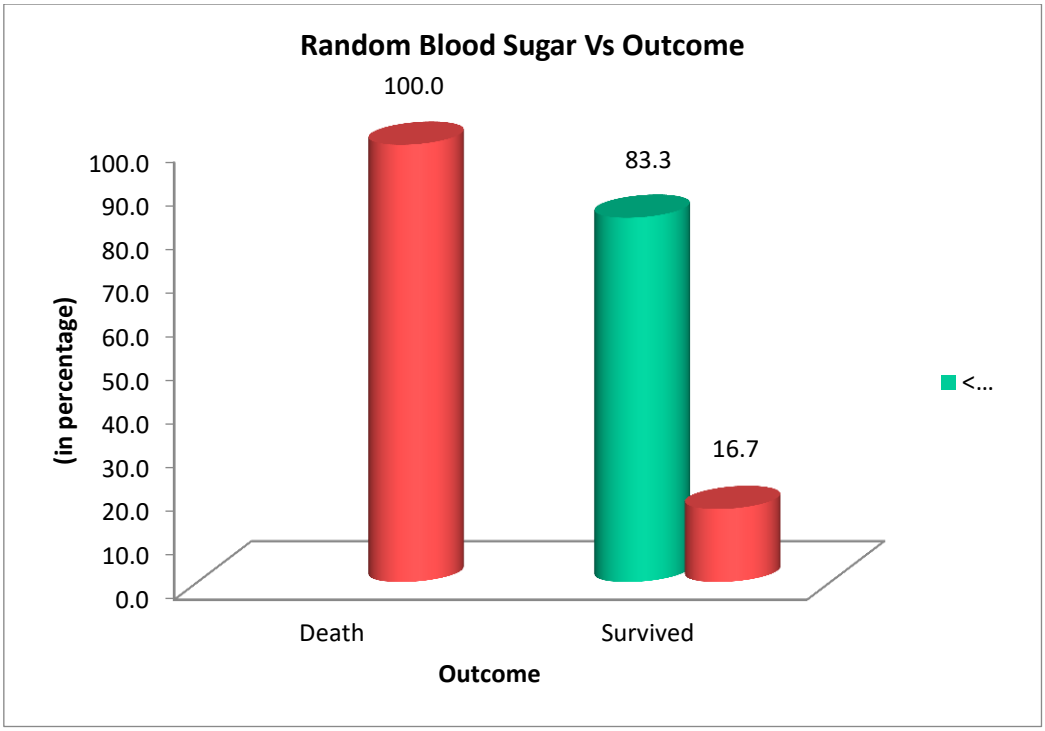


Age (in yrs)	
N	40
Mean	35.5
SD	10.6
Minimum	19
Maximum	61

Age group (in yrs)	No. (%)
≤30	14 (35.0)
31 – 40	15 (37.5)
41 – 50	7 (17.5)
>50	4 (10.0)
Total	40 (100.0)

COMMENTS

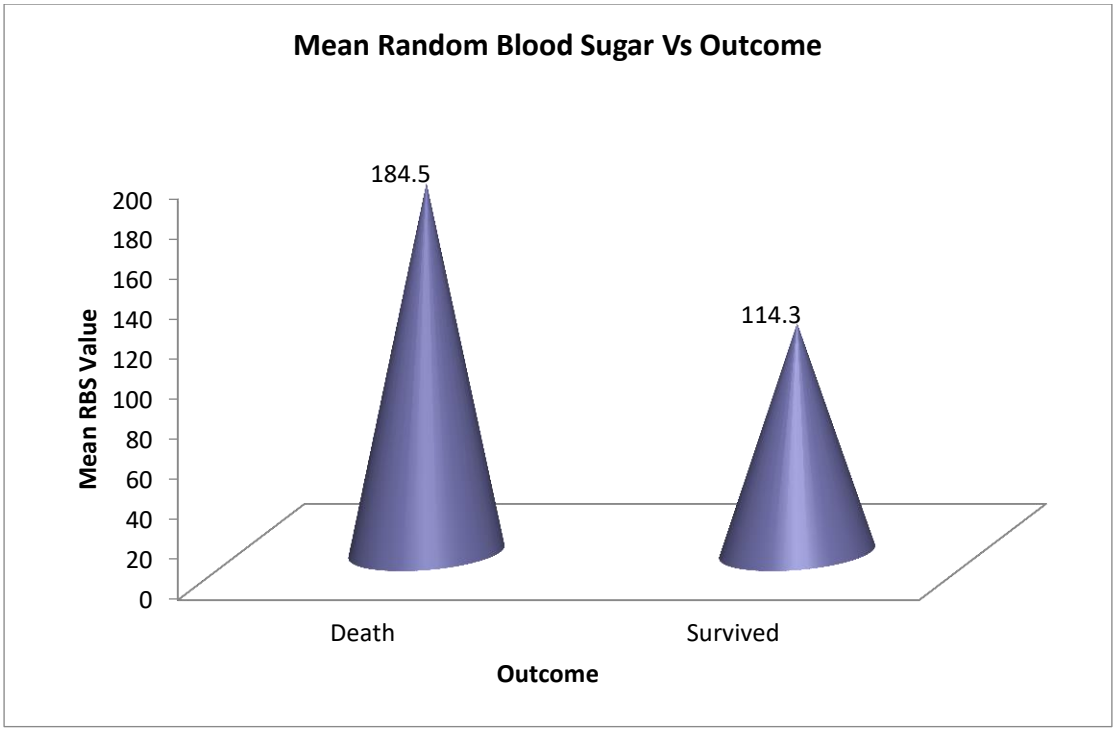
The mean age among the study population (n= 40) is 35 yrs. The minimum age is 19yrs and maximum age included in study was 61yrs.



Random Blood Sugar – at the time of admission	Outcome	
	Death	Survived
	No. (%)	No. (%)
<140	-	5 (83.3)
≥140	34 (100.0)	1 (16.7)
Total	34 (100.0)	6 (100.0)
P value	<0.001	

COMMENTS

Among 40 patients, 34 patients died in this study. The random blood sugar at the time admission for those who died were found to have > 140 mg/dl. 6 patients were survived in this study and among them, the random blood sugar at admission was > 140 in 1 patient and < 140mg/dl in 5 patients.



Random Blood Sugar – at the time of admission	Outcome	
	Death	Survived
N	34	6
Mean	184.5	114.3
SD	35.2	41.0
Minimum	144	68
Maximum	285	184

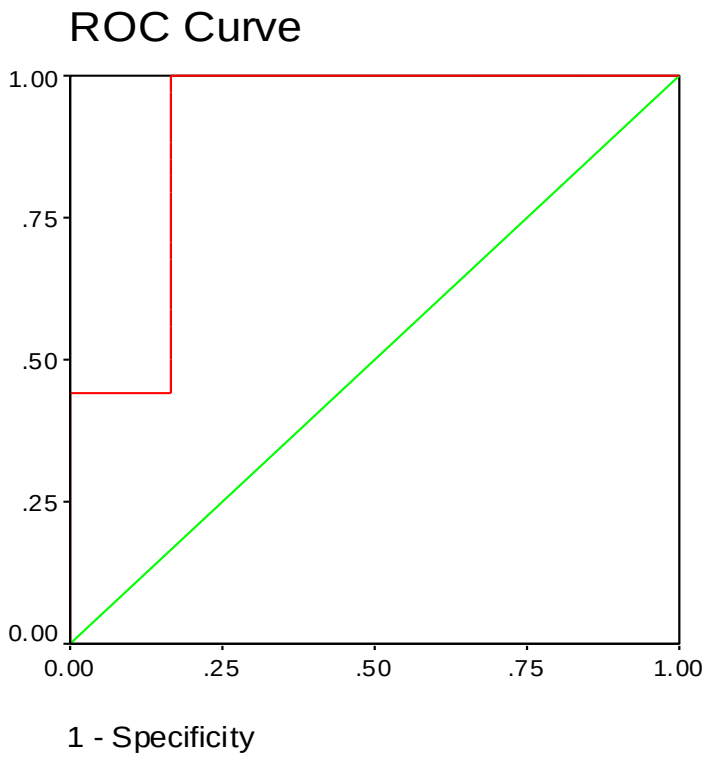
COMMENTS

The mean random blood sugar among patients who died was 184 mg/dl and those who survived was 114mg/dl. This indicates that the elevated random blood sugar was a independent predictor of mortality in aluminium phosphide poisoning.

Correlation between Random Blood Sugar – at the time of admission and Duration of Hospital Stay

	Mean	**Standard Deviation**	**Correlation Co-efficient**	**p-value**
Random Blood Sugar	173.9	43.7	-0.396	0.012
Duration of Hospital Stay (in hrs)	78.7	70.3		

ROC data										
Area under the ROC curve 0.907								**p=0.002**		
RBS	**Sensitivity**	**95% CI**	**Specificity**	**95% CI**	**PPV**	**95% CI**	**NPV**	**95% CI**	**+LR**	**-LR**
144.5	97.1	84.1 – 99.9	83.3	35.9 – 99.6	97.1	84.6 – 99.5	83.3	41.2 – 97.3	5.82	0.04



COMMENTS:

Picture and table shows ROC curve and its relation to the results.

DISCUSSION

Forty patients (06 women and 34 men) with AlP poisoning were included in the study. The mean age was 35.5 ± 10.6 years (range: 19–61).

Most patients were in their second and third decade of life (Table 1). Six patients survived (15%) and 34 patients expired (85%). AlP poisoning followed deliberate ingestion in all patients.

44.4% of patients were poisoned with only one tablet of AlP, delivering 1680 mg AlP. The interval time to treatment between ingestion and arrival at the hospital in survived and non-survived were 4.2 (±0.7) h and 2.8 (±0.3) h, respectively. There were no significant differences between survived and non-survived groups according to age, gender, and time to treatment.

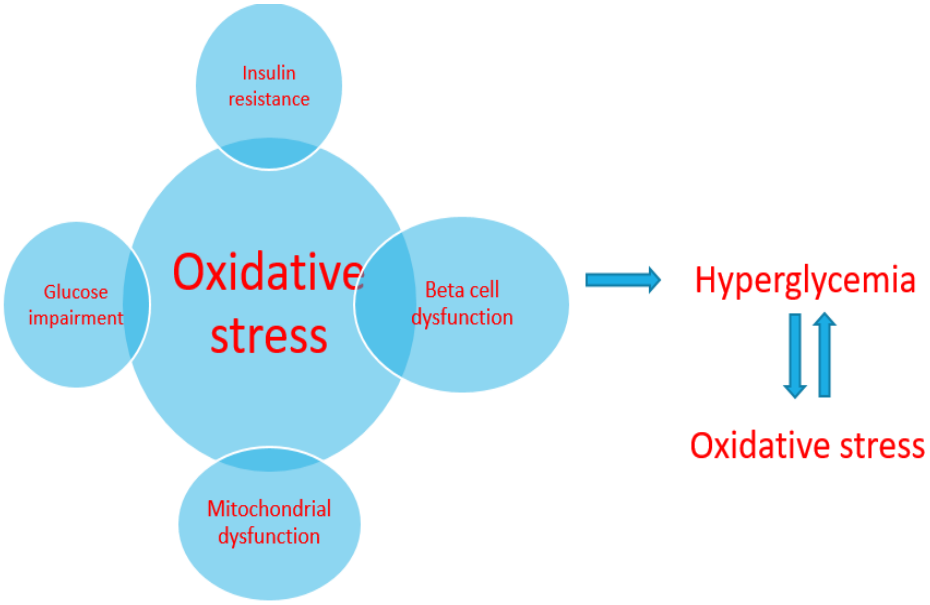
All patients required endotracheal intubation and mechanical ventilation. There was significant correlation between blood glucose level at the time of admission and outcome of the particular patient.

The mean blood glucose levels in survived and expired patients were 114.3 ± 41.0 mg/dL and 184.5 ± 35.20 mg/dL, respectively , a difference that reached statistical significance (P = 0.001). thirty Six (85%) of nonsurvived and 06 (15%) of survived patients had blood glucose levels greater than 140 mg/dL. After adjusting according to age,

gender, ingested dose, pH, and HCO3. concentration, the odds ratio for hyperglycemia as a risk factor for death was 5.7 (CI 95% = 1.4–23.4).

Several studies on the effect of aluminium phosphide poisoning on blood glucose levels have shown fluctuations in blood glucose levels. Following mechanisms are reported –

1. Chugh, et al showed a significant rise in plasma cortisol(> 1048 nmol/L) in 40% cases. Post mortem findings showed mild to moderate adrenal cortex changes. This involvement of adrenal axis provides an explanation for derangement in glucose homeostasis.
2. In addition, this poisoning has been associated with acute pancreatitis lead on to hyperglycemia.
3. AlP induce oxidative stress and increase extramitochondrial release of free oxygen radicals resulting in lipid peroxidation and protein denaturation of cellular membranes in various organs.



- The above mechanisms may explain the fact that hyperglycemia is a poor prognostic factor in aluminium phosphide poisoning.
- The administration of Hyperinsulinemia euglycemia therapy has an advantage in improving mortality in AlP posoining.
- It improves inotropy and peripheral vascular resistance and reverse acidosis by improving myocyte carbohydrate uptakeand utilisation.
- Thus, oxidative stress can be possibly ameliorated by management of hyperglycemia and changes or disruptions in these mechanisms may reduce the risk of insulin resistance and the development of hyperglycemia and, furthermore, may have a potential role in its treatment

Previous research work has shown similar results. O Mehrpour et al., reported that non-survivors of AIP poisoning had a statistically significant tendency towards hyperglycemia when compared with survivors, suggesting that hyperglycemia may be used as a marker of AlP poisoning severity and may be a useful prognostic tool in evaluating and managing this particular poisoning.

Hence, this study correlates the effect of hyperglycemia and mortality in aluminium phosphide poisoning and suggests that random blood glucose monitoring may be useful in guiding risk assessment and treatment of AIP poisoning.

Insulin remains the obvious treatment for hyperglycaemia and lowering blood glucose levels to 80-110 mg/dl has a pivotal role in the treatment of such patients. Prevention of the inflammatory process and insulin resistance may also be important for the improvement of critically ill patients with acute hyperglycaemia. Although the role of treatment of hyperglycaemia with insulin and metformin has been evaluated in critically ill patients in the studies by Goldberg and Mojtahedzadeh, none of these modalities was performed in poisoning cases. A large randomized controlled trial study is necessary to affirm the role of insulin or metformin treatment in admission hyperglycaemia induced by severe poisoning.

Although poisoning cases with toxic agents which produce hypoglycaemia were excluded from our study, hypoglycaemia was also observed in some of the patients. However, there was no relationship between hypoglycaemia and severity of poisoning. We have no explanation for this. Since hypoglycaemia recovered after 0.5-1 g/kg infusion of hypertonic dextrose, the poor nutrition of suicidal patients may be one of the reasons (because of an argument with their family they had not eaten lunch or dinner before the suicide attempt).

In conclusion, acute poisoning-induced hyperglycaemia may be a good predictor of severity of poisoning and clinical outcome

CONCLUSION

The importance of the findings of this study emphases on the significant negative effect of hyperglycemia on admission in patients with aluminium phosphide poisoning. The administration of Hyperinsulinemia euglycemia therapy has an advantage in improving mortality in AlP posoining. It improves inotropy and peripheral vascular resistance and reverse acidosis by improving myocyte carbohydrate uptakeand utilisation. Thus, oxidative stress can be possibly ameliorated by management of hyperglycemia and changes or disruptions in these mechanisms may reduce the risk of insulin resistance and the development of hyperglycemia and, furthermore, may have a potential role in its treatment.

PROFORMA

Name:

Age / Sex:

Occupation:

Presenting complaints:

Past History:

H/o DM, HT, CKD, CVD, DRUG INTAKE, CAD, Thyroid disorders, Alcohol intake

Clinical Examination:

General Examination:

Consciousness,

Pallor,

Jaundice,

Clubbing,

Lymphadenopathy,

Hydration status

VITALS:

PR

BP

RR

SpO2

SYSTEMIC EXAMINATION:

CVS:

RS:

ABDOMEN

CNS:

Laboratory investigations:

Random blood sugar at the time of admission

1) Complete blood count

2) Renal function test

3) Liver function test

4) Urine routine

5) Electrocardiogram

6) Chest X ray

7) USG abdomen

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S.NO	NAME	AGE	SEX	DIAGNOSIS	RANDOM BLOOD SUGAR AT THE TIME OF ADMISSION	OUTCOME	DURATION OF HOSPITAL STAY
1	Murugesan	44	M	Alumium Phophide Poisoning	150mgs%	Death	2 days
2	Sathya	48	M	Alumium Phophide Poisoning	184mgs%	Survived	10 days
3	Ganesan	32	M	Alumium Phophide Poisoning	155mgs%	Death	5 days
4	raja	30	M	Alumium Phophide Poisoning	204mgs%	Death	16 Hours
5	sivaraman	32	M	Alumium Phophide Poisoning	188mgs%	Death	2 Days
6	bhuvana	25	F	Alumium Phophide Poisoning	177mgs%	Death	1 days
7	Arul	20	M	Alumium Phophide Poisoning	148mgs%	Death	5 days
8	Sangavi	21	F	Alumium Phophide Poisoning	166mgs%	Death	10 days
9	Ramasamy	25	M	Alumium Phophide Poisoning	104mgs%	Survived	6 days
10	Sampath	49	M	Alumium Phophide Poisoning	135mgs%	Survived	5 Days
11	christopher	40	M	Alumium Phophide Poisoning	257mgs%	Death	6 Hours
12	rani	45	F	Alumium Phophide Poisoning	85mgs%	Survived	5 Days
13	pandy	30	M	Alumium Phophide Poisoning	147mgs%	Death	2days
14	muthumeena	30	F	Alumium Phophide Poisoning	144mgs%	Death	7 Days
15	ananthi	30	F	Alumium Phophide Poisoning	222mgs%	Death	1 days
16	sumathi	32	F	Alumium Phophide Poisoning	68mgs%	Survived	3 Days
17	rajesh	44	M	Alumium Phophide Poisoning	151mgs%	Death	3 days
18	mani	61	M	Alumium Phophide Poisoning	160mgs%	Death	2 days
19	Murugesan	19	M	Alumium Phophide Poisoning	166mgs%	Death	3 days
20	palani	47	M	Alumium Phophide Poisoning	198mgs%	Death	1 days
21	kumar	40	M	Alumium Phophide Poisoning	170mgs%	Death	8 days
22	nallathambi	26	M	Alumium Phophide Poisoning	180mgs%	Death	7 Days
23	sivakumar	31	M	Alumium Phophide Poisoning	221mgs%	Death	12 Hours
24	muniyasamy	32	M	Alumium Phophide Poisoning	200mgs%	Death	10 Hours
25	mothilol	36	M	Alumium Phophide Poisoning	168mgs%	Death	4 Days
26	balu	39	M	Alumium Phophide Poisoning	220mgs%	Death	5 Hours
27	kannan	38	M	Alumium Phophide Poisoning	180mgs%	Death	10 days
28	rajendhiran	20	M	Alumium Phophide Poisoning	188mgs%	Death	1 days
29	thangapandy	29	M	Alumium Phophide Poisoning	255mgs%	Death	3 Hours
30	abbas	30	M	Alumium Phophide Poisoning	210mgs%	Death	5 Days
31	shyam	31	M	Alumium Phophide Poisoning	155mgs%	Death	1 days
32	naresh	34	M	Alumium Phophide Poisoning	110mgs%	Survived	4 Days
33	sampath	35	M	Alumium Phophide Poisoning	145mgs%	Death	2 days
34	perumal	36	M	Alumium Phophide Poisoning	166mgs%	Death	1 hours
35	kumeresan	52	M	Alumium Phophide Poisoning	190mgs%	Death	4 Days
36	karupaiah	61	M	Alumium Phophide Poisoning	210mgs%	Death	1 Days
37	dinesh	52	M	Alumium Phophide Poisoning	147mgs%	Death	6 days
38	hameed	36	M	Alumium Phophide Poisoning	285mgs%	Death	2 Hours
39	pandiyan	20	M	Alumium Phophide Poisoning	155mgs%	Death	2 Days
40	suresh	41	M	Alumium Phophide Poisoning	195mgs%	Death	1 Dyas

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Period of Study	:	2015-2018
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	Hyperglycemia in acute aluminium phosphide poisoning as a potential prognostic factor
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